

# PROCESS FOR CONTROLLING THE HYDRATE MIX OF A COMPOUND

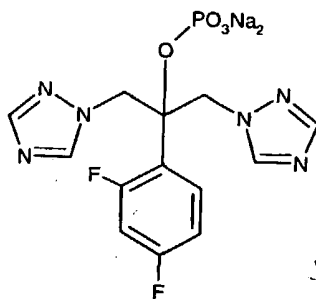
This application claims priority from U.S. Provisional Application Serial No. 60/399,491 filed 29 July 2002, which claims priority from United Kingdom Patent Application Number 0216515.7, filed 16 July 2002, which are hereby incorporated by reference in their entireties.

## Field of the Invention

This invention relates to a process for controlling the hydrate mix of a compound, or a composition comprising the compound, the compound being capable of forming a plurality of hydration forms of differing stability. More particularly, this invention relates to a process for controlling the hydrate mix of a compound, or a composition comprising the compound, the compound being capable of forming a plurality of hydration forms of differing stability and also of dissolution to give a solution that, when frozen below the eutectic point, is a eutectic mixture.

## Summary of the Invention

An example of a compound which exhibits a plurality of hydration forms is the disodium salt of fosfluconazole (hereinafter DSFF). DSFF is disclosed in WO97/28169 and has the following structure:



with  
hydrate  
tri + monohydrates

A number of hydration states of DSFF have now been found to exist and it is hypothesised that these are the dodecahydrate (33.4% w/w water), hexahydrate (20.1% w/w water), trihydrate (11.2% w/w water) and monohydrate (4.0% w/w water) forms. The anhydrous form of DSFF is believed to be amorphous. While the tri- and hexahydrate forms of DSFF are both chemically and thermally stable, it has been found that certain hydrate forms, such as the dodecahydrate, exhibit physical and/or chemical instability. While not wishing to be bound to any particular theory, it is believed that the eutectic form of DSFF is a dodecahydrate and it has been found that this dodecahydrate form is thermally unstable. Furthermore, it has been discovered that forms of DSFF which have a water content of from 4.0% w/w to 11.2% w/w are also chemically unstable. It is hypothesised that such a hydrate mix is a combination of tri- and monohydrate forms. Additionally, it has been found that samples of DSFF having a water content above the hexahydrate stoichiometry (20.1% w/w) collapse in a manner consistent with equilibration to the hexahydrate and water. Indeed, any composition comprising an unstable hydrate form, despite possibly containing stable forms, will decompose.